# Neural Implants Come of Age

THE symbiotic union between man and machine has been a subject of great fascination to scientists and science fiction writers alike for generations. But for researchers such as Satinderpall Pannu of Livermore's Engineering Directorate, integrating nanometer-size devices with biological systems and studying the interface between them is a daily reality. In 2009, he and his team set the stage for a new generation of neural implants with the design and fabrication of an artificial retina. The device—the first high-density, fully implantable neural prosthetic ever produced—restores a sense of vision to people who have lost their sight because of ocular disease. Since then, Pannu and his team have continued to enhance the technology, which promises to dramatically improve the lives of patients with debilitating conditions caused by injury or neurological disease.

Keys to the success of this new class of implants are advances made at Livermore in the area of nano- and microfabrication techniques and in the use of novel materials that make the devices both biocompatible and fully implantable for long-term use. Moreover, the implants promise to do more than just stimulate neural tissue. They will record electrical and even chemical signals for the first time, creating a feedback mechanism that allows the stimulation to be fine-tuned for each patient. "These devices are a real game changer," Pannu says. "Once we understand what fully implantable prosthetics can do, the floodgates to innovation are open."

Neural implants, or prosthetics, are a class of devices that communicate with the nervous system. An electronics package in each device activates an array of tiny electrodes that interface directly with healthy neurons in the body. Signals produced by the electrodes bypass damaged areas of the brain or part of the nervous system to restore function, block pain, or prevent seizures. Someday, these devices may even be used to treat depression and other ailments.

The first widely used neural prosthetic was the cochlear hearing implant in the early 1980s, which provides a sense of sound to people with severe hearing impairment. Since the late 1990s, implants for the brain and spinal cord have been developed with varying degrees of success. Some help prevent seizures in patients with epilepsy and Parkinson's disease. Spine implants are being used for pain control, and other devices stimulate peripheral nerves and muscles. Although these devices have dramatically improved many people's lives, they are limited in terms of performance compared to the promise held by technologies now under development. Except for the artificial retina, today's implants operate with a handful of electrodes and an electronics package the size of a deck of cards, which causes significant complications during and after surgery. Moreover, the lifetime of newer devices is short because the electrodes are made of silicon, a rigid material prone to breaking.

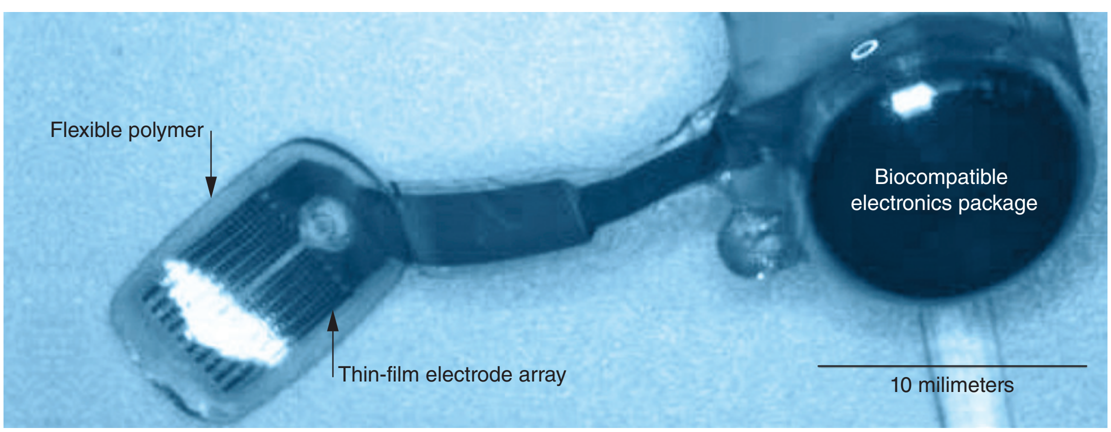
## Building a Better Implant

The Livermore researchers wanted to take implant technology to a new level—in particular, by making electrodes smaller and more flexible so that more can be packed in ever-smaller packages. A recent advance by the team seals the components in a self-contained, wireless device that can be placed inside the human body without causing adverse reactions. The package, miniaturized to fit in an area less than 10 millimeters in diameter and 4 millimeters tall, contains a microelectrode array, inductive coils to power the device, and electronics hermetically sealed inside a metal container brazed onto a biocompatible ceramic disk.

The microelectrodes at the heart of this technology are embedded in a flexible polymer, which allows the device to move naturally and conform to the live tissue in which it is implanted, such as the brain. The device can be custom designed to the shape needed for each clinical requirement. Once implanted, the delicate-looking but robust microelectrode array can last for years, possibly even decades, because polymer is more compatible with the human body than silicon. The Livermore technology is the only thin-film electrode array approved for long-term human implantation. According to electrical engineer Angela Tooker, polymers have more commonly been used as insulating materials. "Electronics are made of metal, and getting them to work with polymers is a specialty we've developed at Livermore."

Work on the implant technology is performed at the Center for Micro- and Nanotechnologies in the polymer fabrication laboratory. The center's mission is to invent, develop, and apply micrometer- and nanometer-scale technologies in support of the Laboratory's missions. Specialized equipment available at the facility includes metal deposition systems and machines that etch and pattern electrodes. Other tools can position components within an accuracy of a few micrometers, and wire bonders can electrically connect them. (See the movie at www.llnl.gov/news/video/retina.mov for a look at the artificial retina fabrication process.) Using this equipment, Livermore engineers can design new arrays quickly when the demand arises. "Someone else would have to find a medical device foundry that has these capabilities," says Pannu, who heads the center. "Worldwide, only a couple of such facilities are available."

Equally important is the group's expertise in devising and fabricating such complex devices. Kedar Shah, the mechanical engineer leading the implant assembly, explains the challenge involved in safely integrating implant components into a device the size of a small button. "The electronics package is only 3 millimeters tall," he says. "Within this small unit, we pack a couple electronic chips and dozens of passive components, such as capacitors, resistors, and diodes. But these components are often made of toxic materials, so we have devised methods to seal them off to prevent contact with the body." The body's moisture cannot

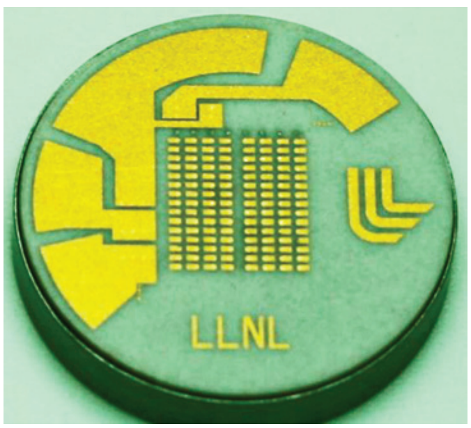



The most recent design of Livermore's artificial retinal implant has an array of 240 thin-film microelectrodes inside a microelectronics package.

touch the electronics either because it would short them out. The package is thus hermetically sealed, and conduits are incorporated to transfer electric signals to the outside without allowing particles to escape.

The artificial retina demonstrated that the Livermore team could meet the design challenge, successfully transitioning the implant from research idea to application. The team received the 2009 Editor's Choice Award in *R&D Magazine*'s annual competition for the top 100 technologies and a 2010 Breakthrough Award for Innovation from *Popular Mechanics*. Since then, the team has continued to improve the technology. Implants now pack hundreds of microelectrodes, compared with 16 and 60 electrodes, respectively, for the first two generations of the artificial retina. The team is now searching for industrial partners with the expertise to run long-term clinical trials—the next step toward obtaining approval from the Food and Drug Administration for the new generation of implants.

"The most recent devices we're developing cannot be put in humans yet, but we design them with this goal in mind," says chemical engineer Vanessa Tolosa. "That's where the collaborators come in. We need to work with neuroscientists and clinicians to determine how they would use the implants and what conditions a device would experience over its lifetime. Then we can design the technology to meet those requirements."

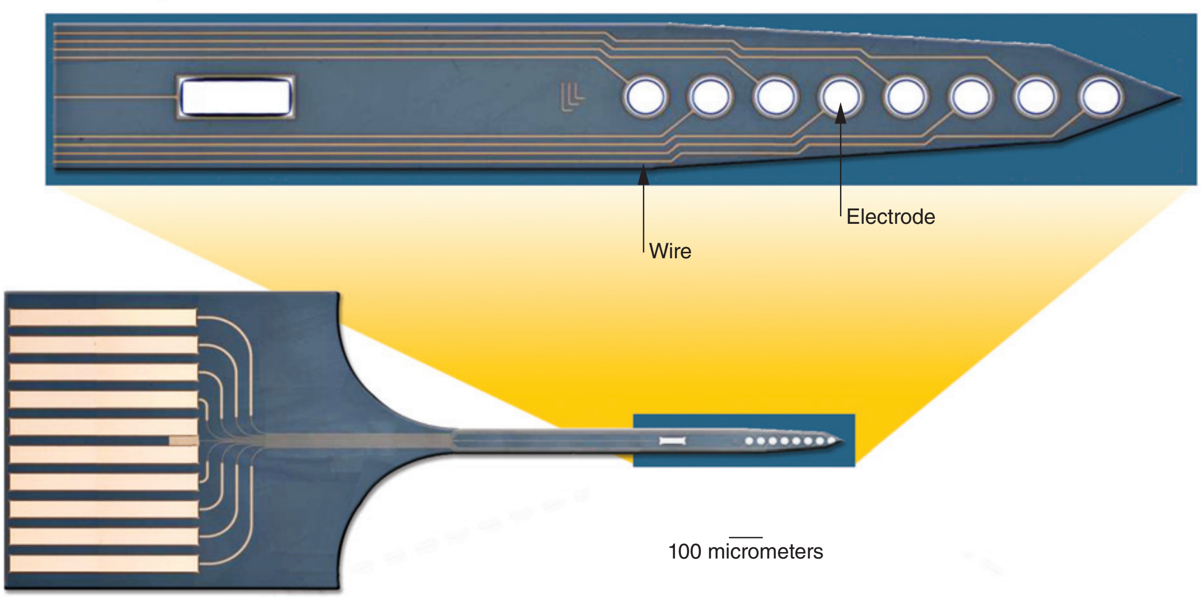



A biocompatible ceramic disk such as the one shown here protects the electronics package for a neural implant from the harsh environment of the body.

## Implants under Development

The next application of the neural interface will be an implant to provide bladder control for people with spinal cord injury. This device, which is being developed with funding from the University of California Office of the President, will stimulate nerves in the bladder to contract the appropriate muscles. The system will have about 10 times the number of electrodes in an electronics package 10 times smaller than any previous system. Researchers at the University of California at Santa Cruz are collaborating with the Livermore team to design the wireless electronics. The Huntington Medical Research Institutes in Pasadena, California, will conduct animal trials with the new interface.

The Laboratory is also working with the National Institutes of Health to devise an improved auditory nerve implant. To implant

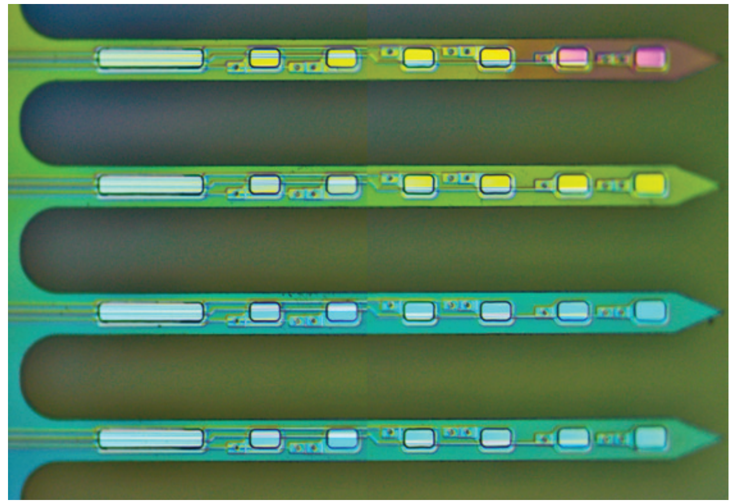



A thin-film electrode array uses complex electronics connections to stimulate and record neural signals.

the commercially available cochlear prosthetic, a surgeon must first remove a small part of a patient's skull and insert the device in the cochlea, a bony membrane inside the ear. The electronics device, however, is placed outside that membrane—not inside the human body—with nerve fibers lying on the opposite side of the bone. As a result, the electric signal's amplitude must be high enough to penetrate the bone and stimulate the neurons on the other side, which causes the current to spread and thus distorts the signal. The fidelity of the device is poor, making it difficult for patients to discern conversations in a noisy environment.

Livermore's auditory device will have hundreds of electrodes, compared with only 19 in the most advanced cochlear implant. "We are designing the implant to go into the auditory nerve directly," Pannu says. "The nerve is approximately 1.5 millimeters long, and we can put hundreds of electrodes along each nerve."

Pannu's team is also working on a Laboratory Directed Research and Development project to design a neural implant that can treat depression with deep brain stimulation. Not only will the device record and stimulate brain signals, but it will also use microfluidic channels for drug delivery.



This multipronged thin-film electrode array records and stimulates brain signals. The device offers a wide range of treatment applications, from Parkinson's disease to seizures or depression.

## Offering Hope for Future Treatments

According to Pannu, implants such as the bladder-control device are but a first step toward more advanced technologies. For example, peripheral nerve interfaces could someday give amputees fine motor control over artificial limbs. "Designing such devices is only a matter of adding complexity," he says. The most advanced technologies available today allow people who have lost an arm, for instance, to control a robotic limb by twitching muscles in their chest—a motion that is very unnatural. "What they really need is a peripheral nerve interface," Pannu says, pointing to a video of a veteran who lost her arm in Iraq. "For her, the nervous system is intact except for where the arm was severed. The peripheral nervous system is there; the neurons are there; the brain is sending all the signals. What we need to do is place a microelectrode array in the peripheral nerves to pick up and decode the signal that tells the fingers to move."

Another potential application is to adapt the recording mechanism in electrode arrays to enhance the performance of brain implants for Parkinson's patients. Existing implants are the equivalent of white noise generators for the brain, shocking the brain at all times to prevent occasional seizures. The proposed device would instead monitor electric signals in the hippocampus and pick up abnormal activity to disrupt a seizure before it happens. The highly sensitive device could also track chemical signals, an important feature for brain activity involving neurotransmitters.

This entire field of interfacing human-made devices with neural tissue is still in its infancy. Implementing many of the new technologies will take at least 20 years, Pannu estimates, given the long process of finding research partners and running clinical trials. Scientists will continue to work on better understanding how neural stimulation affects different parts of the body so they can fine-tune the implants for increasingly complex situations. But judging by the progress made since the artificial retina was developed, the possibilities for progress appear to be endless.

"We really believe in the technology," says Tolosa, who is working on the deep brain stimulation project. "We've already seen what it can do in a short period of time, and we think the potential applications on the horizon are not just far-off dreams. We can make them happen provided we have the resources to support this work."

Until then, the researchers take great satisfaction from knowing they are making a difference in people's lives, and—perhaps even more importantly—they are giving many patients a precious gift: hope. "We get e-mails from parents whose children have retinitis pigmentosa," Pannu says. "They know their kids will go blind because no therapies are available to help them. They're desperate. The artificial retina offers hope that there will be a better future for their children."

*—Monica Friedlander*

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